REMARKS

Claims 1-17 are pending and have been rejected in an office action mailed on April 22, 2003. After the present amendment, claims 7, 13 and 14 are canceled, and claims 1-6, 8-12 and 15-17 remain pending. The recitation "that can be present transiently at the cell surface via a GPI anchor" added to claim 1 is supported, for example, in the last 5 lines of page 3 through page 4. The term "GPI anchor" is supported, for example, by example 7 starting in the middle of page 14. The phrase "hybridoma supernatants" is supported, for example, on page 7 lines 15 to 24. No new matter has been added. Reconsideration and allowance in view of the amendments and arguments respectfully are requested.

Rejections - 35 USC 112

The Examiner has "maintained in part" rejections of claims 1-18 on alleged indefiniteness grounds. The Examiner argues on page 3 of the office action that "it is not clear from step a) whether the host cell is in vitro or in vivo" and that the claims may "read on polypeptides which may or may not be secreted."

In response, claim 1 has been amended to recite "expressed in vivo." Furthermore, the claim recites polypeptides "that can be present transiently at the cell surface via a GPI anchor," which only happens with polypeptides that have a secretion sequence or leader sequence, as indicated on page 3, lines 35-38 of the specification. The Examiner mentioned the possibility of "polypeptides secreted from the host cell" and suggested that the claimed polypeptide may be "linked to a sequence" that allows such cell efflux, on page 3, bottom of the office action. The amended claim 1 inherently describes the sequence and claim 2, as amended now states specifically the use of "a secretion signal leader sequence." Applicants point out that endogenous cleavage enzymes exist within the cell, which allow for release of the extracellular region of the polypeptide, which simulates an optimal immune response. Applicants also thank the Examiner for suggesting the term "present" to describe location of the polypeptide at the cell surface, rather

than bound per se to the cell surface. Applicants point out that page 4 lines 24-26 of the specification describe a GPI anchor that "is easily cleaved from the cell surface."

The Examiner further argued that "whether step b) includes an in vitro step separate from step a)" is unclear, on the middle of page 4 of the office action. Amended claim 1 now recites that step a) is an in vitro step and that step b) involves independent cloning into a vector prior to in vivo use. The amended claims now clarify that, step a) is an in vitro assay system and step b) is an immunization step. Consequently, claim 7 has become redundant and is omitted for this reason.

The Examiner argued that (page 4 top, office action) the step of "antibodies are removed from the animal" is missing. Amended claim 1 c) now recites this step in part.

The Examiner also argued on page 5 that a reference to "step b) " in claim 1 is indefinite and that "there is no antecedent basis for 'the expression vector.'" Amended claim 1 lacks a reference to step b) and added "expression vector" to step b).

In view of the clarifying amendments to claims 1 and 2, and the explanation above, the Examiner respectfully is requested to remove this rejection.

Rejections - 35 USC 103

On page 5 to page 10, claims 1-3, 5,-7, 9-11 and 14-15 have been rejected on alleged obviousness grounds over Content et al combined with other references, and claims 4, 8, 12, 13 and 16 over Content et al. further in view of additional references.

Amendments made to claim 1 provide a combination of elements that is not found in these references. In particular, the vector described in independent claim 1 is useful for both immunization and screening, without having to isolate the subject polypeptide. Applicants note that the transiently infected cell itself represents a solid phase. Furthermore, inclusion of the cleavable or partially cleavable cell membrane anchoring sequences that are replaced by a GPI

anchor offers a further secretion signal to allow most polypeptides to be brought io the cell surface, for binding there via the GPI anchor. This system allows the use of any polypeptide without having to isolate the polypeptide.

These new features are not described or suggested in any of the cited references, and allow a more optimal presentation of a native polypeptide for both stimulation of an immune response within the animal, as well as screening for antibodies made by mammalian cells in vitro. The novel features and advantages for the recited antibody generation and screening method provide savings in time and money, particularly since no polypeptide need be isolated and the generation of immunogen (immunization vector with the cDNA encoding the antigen) takes only 10-14 days.

The term "expressed transiently in vitro" in the claims further distinguishes the claimed invention from the cited art. Advantageous savings accrue from the use of transiently transfected cells instead of stably transfected cells for in vitro assay of antibodies via CELISA or flow cytometry (see specification on p. 15, line 25-p. 16 line 25, p. 17 lines 6-14; and p. 17 line 14 to p. 18 line 18, respectively).

New cited art Kilgannon lacks elements of the amended claims and cannot form a prima facie obviousness rejection. Kilgannon et al. describe ICAM-4/GST fusion proteins, wherein GST can be used as a detection signal for detecting the ICAM-4 fusion protein. Now that claim 1 (a) has been excluded, the Kilgannon patent has no more relevance to the new claim 1 (a). The same applies to the patent from Letesson et al., which also has no more relevance to the new claims.

Whitehorn et al., indeed used a GPI anchor, but relies on separation of the construct from expressing cells through cleavage with phospholipase C enzymes and isolation of the recombinant polypeptide using an antibody targeting the signal sequence at the C-terminus of the released extracellular domain. Although amended claim 1 (a) describes a GPI anchor, the claimed system does not require isolation of polypeptide from the cells. The claimed system relies instead on release of the polypeptide from the cells of immunized animals by endogenous enzymatic cleavage. This allows a more optimal immune response as described in amended claim 1 b).

The claimed assay system recited in 1 (c) uses the cell-based expression system of

amended claim 1 (a) and thus differs from that described by Whitehorn et al.

In contrast to the descriptions in the previous three cited patents that initially have to isolate recombinant protein, Content et al. administers plasmid vectors rather than recombinant proteins into animals. However, their test system necessitates binding of expressed polypeptide to a solid support following lysis of transfected cells. This method again differs from that presented in the amended claims. Any possible motivation provided by Content et al. to use a DNA immunogen when combined with the methods of Kilgannon et al. would not compare with the novelty of the claimed system, which utilizes the same vector for immunization and for the assay. For immunization, the surface-expressed recombinant polypeptide is cleaved by endogenous enzymes within the animal to stimulate an optimal immune response. For the assay, the GPI-linked polypeptide is used *in vitro* to test for the presence of antibodies in the serum and hybridoma supernatants using transiently transfected cells as a solid phase system. Thus the same expression vector can be used for both purposes, without the need to isolate the recombinant protein. This combination is lacking in the references.

The several combination of features and advantages of their use as described above are not presented in any reference either alone or in combination. Reconsideration and allowance in view of the amended claims respectfully are requested.

CONCLUSION

In view of the foregoing, Applicant respectfully requests the Examiner to withdraw the rejections against all pending claims. The Examiner is invited to contact the undersigned attorney to resolve any issues, in order to expedite the prosecution of the application.

Respectfully submitted,

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